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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,424	06/28/2002	Muhammed Majeed	108064-00049	2480

4372 7590 07/28/2003

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EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/28/2003 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/926,424	Applicant(s) MAJEED ET AL.	
	Examiner Shaojia A Jiang	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *82-129,144-151,162-169,174 and 175* is/are pending in the application.

4a) Of the above claim(s) *82-129 and 163-169* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *144-151,162,174 and 175* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a 371 (national stage entry) of PCT/US00/08217 International Filing Date: 04/28/2000, and is a continuation of 09/302,510.

As indicated in the previous Office Action, Applicant's preliminary amendment in Paper No. 6, submitted October 30, 2001 is acknowledged, wherein claims 1-85 have been cancelled and claims 86-176 are newly submitted.

Applicant's preliminary amendment in response to the Restriction Requirement (March 12, 2003), submitted May 12, 2003 in Paper No. 9 is acknowledged, wherein claims 130-143, 152-161, 170-173, and 176 have been cancelled.

Currently, claims 86-129, 144-151, 162-169, 174 and 175 are pending in this application.

Election/Restrictions

Applicant's election with traverse of the invention of Group IV, Claims 144-151, 162 and 174-175 drawn to methods for prevention and treatment of an autoimmune disease employing the particular compositions, in Paper No. 9, submitted May 12, 2003 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 86-129 and 163-169 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 144-151, 162 and 174-175 will be examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 144-147 and 174 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to the methods for the **prevention** of an autoimmune disease in a human or animal. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The instant invention pertains to the method the prevention of an autoimmune disease in a human or animal.

The state of the prior art: The skilled artisan would view that the treatment to prevent an autoimmune disease in a human or animal totally, absolutely, or permanently, is highly unlikely, not even occurring at the first time.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or lack thereof in the art: The skilled artisan would view that the treatment to prevent an autoimmune disease in a human or animal totally, absolutely, or permanently is highly unpredictable, and not even occur at the first time is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples: In the instant case, **no** working examples are presented in the specification as filed showing how to prevent an autoimmune disease in a human or animal totally, absolutely, or permanently, not even occurring at the first time.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed

above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 162 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the treatment of an autoimmune disease in a human or animal disclosed in the specification by administering the instant compounds herein, does not reasonably provide enablement for **preventing** an autoimmune disease in a human or animal by administering the compounds recited in the claims herein for the same reasons as discussed above (see supra page 3-4).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 144-151, 162 and 174-175 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Nagasawa et al. (JP 0428809, PTO 1449 submitted October 30, 2001) in view of Shao et al. (XP-000912127, PTO 1449 submitted October 30, 2001).

Nagasawa et al. discloses that boswellic acids such as β–boswellic acid, acetyl-β–boswellic acid, 11-keto-β–boswellic acid, and acetyl-11-keto-β–boswellic acid are useful in pharmaceutical compositions and in the method for treatment of autoimmune diseases including systemic erythematosis and articular rheumatism in humans since β–boswellic acids exhibit a good and complemental activity-inhibiting autoimmune diseases. See the English abstract.

Nagasawa et al. does not expressly disclose the effective amounts of β–boswellic acids employed in pharmaceutical compositions for methods for treatment of autoimmune diseases in which at least 5% w/w of β–boswellic acid, at least 5% w/w of acetyl-β–boswellic acid, at least 15% w/w of 11-keto-β–boswellic acid and at least 14% w/w of acetyl-11-keto-β–boswellic acid.

Shao et al. discloses that β–boswellic acid (compound 1), acetyl-β–boswellic acid (compound 2), 11-keto-β–boswellic acid (compound 3), acetyl-11-keto-β–boswellic acid (compound 4) are known to be useful in a method of treating inflammatory diseases since these boswellic acids exhibit anti-inflammatory action (see both left and right columns at page 328), and also treating leukemia in human since all four β–boswellic acids possess inhibitory activity against human leukemia H-60 cells (see abstract and the right column of page 328). Shao et al. also teaches that IC_{50} values of these boswellic acids from 1.5 to 7 μm and their dose are known to be dependent on their IC_{50}

values (see the left column of page 328). Shao et al. further teaches that the order of inhibitory activity for these four β–boswellic acids is 4 > 3 > 2 > 1 or IV > III > II > I herein according to their IC_{50} values. See page 330 1st and 2nd paragraphs of the right column, and the right column of page 331.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the effective amounts of β–boswellic acids employed in pharmaceutical compositions for methods for treatment of autoimmune diseases in which at least 5% w/w of β–boswellic acid, at least 5% w/w of acetyl-β–boswellic acid, at least 15% w/w of 11-keto-β–boswellic acid and at least 14% w/w of acetyl-11-keto-β–boswellic acid.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of β–boswellic acids employed in pharmaceutical compositions for methods for treatment of autoimmune diseases in which at least 5% w/w of β–boswellic acid, at least 5% w/w of acetyl-β–boswellic acid, at least 15% w/w of 11-keto-β–boswellic acid and at least 14% w/w of acetyl-11-keto-β–boswellic acid, since the optimization of effective amounts of known active agents to be administered based on the known parameters, their known IC_{50} values and activities according to Shao et al, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Moreover, one of ordinary skill in the art would recognize that autoimmune diseases broadly encompass inflammatory diseases. Hence, the teachings of both Nagasawa et al. and Shao et al. have clearly provided the motivation for the instant invention.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 144-151, 162 and 174-175 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Taneja et al. (EP 0755940, PTO 1449 submitted October 30, 2001).

Taneja et al. discloses that boswellic acids herein such as β–boswellic acid, acetyl-β–boswellic acid, 11-keto-β–boswellic acid, and acetyl-11-keto-β–boswellic acid (Formula I-IV therein at page 3) are useful in pharmaceutical compositions and in the method for treatment of inflammatory diseases including arthritis in humans since these boswellic acids exhibit anti-inflammatory action. See page 2 lines 49-50. Taneja et al. also discloses that the pharmaceutical composition therein comprising these β–

boswellic acids in specifically effective amounts, e.g., 35-55% w/w of β–boswellic acid(which reads on at least 5% w/w), 25-45% w/w of acetyl-β–boswellic acid (which reads on at least 5% w/w), 4-14% w/w of 11-keto-β–boswellic acid, and 3-13% w/w of acetyl-11-keto-β–boswellic acid (see page 5 lines 15-26).

Taneja et al. does not expressly disclose the effective amounts of 11-keto-β–boswellic acid and acetyl-11-keto-β–boswellic acid employed in pharmaceutical compositions for methods for treatment of autoimmune diseases in which at least 15% w/w of 11-keto-β–boswellic acid and at least 14% w/w of acetyl-11-keto-β–boswellic acid.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the effective amounts of 11-keto-β–boswellic acid and acetyl-11-keto-β–boswellic acid employed in pharmaceutical compositions for methods for treatment of autoimmune diseases in which at least 15% w/w of 11-keto-β–boswellic acid and at least 14% w/w of acetyl-11-keto-β–boswellic acid.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of 11-keto-β–boswellic acid and acetyl-11-keto-β–boswellic acid employed in pharmaceutical compositions for methods for treatment of autoimmune diseases in which at least 15% w/w of 11-keto-β–boswellic acid and at least 14% w/w of acetyl-11-keto-β–boswellic acid, since the optimization of effective amounts of known active agents to be administered based on the known effective amounts according to Taneja et al, is considered well in the

competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Moreover, one of ordinary skill in the art would recognize that autoimmune diseases broadly encompass inflammatory diseases. Hence, the teachings of Taneja et al. have clearly provided the motivation for the instant invention.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
July 18, 2003